The Hydrogen Bond between Water and Aromatic Bases of Biological Interest: Rotational Spectrum of Pyridazine−Water

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The free jet millimeter wave spectra of the 1:1 complex between pyridazine and three isotopomers of water (H_2O, D_2O, and $H_2{}^{18}O$) have been assigned. The derived moments of inertia are consistent with a planar structure of the adduct in which one hydrogen of the water molecule is bound to the nitrogen of the aromatic ring, and the "free" water hydrogen is *entgegen* to the ring. Information on the motions of water with respect to the ring is obtained.

Introduction

The study of the intermolecular interactions that drive the solvation of six-membered nitrogenated aromatic rings is of particular importance since they are known to constitute key building blocks of proteins and nucleotides. The investigation of the 1:1 adduct of these molecules with water will be the first step in the understanding of such interactions. Spectroscopic studies of weakly bound intermolecular complexes at conditions of supersonic expansion[1] have provided a wealth of information on the solvation of aromatic molecules[2] and represent a starting point for detailed understanding of macroscopic phenomena. The most direct experimental approach to structure and dynamics in such systems is probably through study of spectra with fully resolved rotational structure.

The prototype system for the study of the interaction of water with an aromatic molecule is benzene−water. The rotational spectra of the 1:1 complex of benzene with several isotopomers of water have been obtained in supersonic expansions.[3,4] These studies show that the water molecule is located above the benzene plane, with both hydrogen atoms pointing toward the π cloud (O−H···π hydrogen bond) and undergoing nearly free internal rotation. Owing to the complexity of its internal dynamics, the geometry of benzene−water is only convincingly explained at a high level of ab initio theory in terms of a quantum mechanical probabilistic structure.[5]

The nitrogenated aromatic molecules we are interested in possess two different proton-acceptor sites: the ring π cloud and the lone pairs on the heteroatoms. Recently, we investigated the pyrazine−water[6] and the pyrimidine−water[7] systems with the free jet absorption microwave technique. In both cases the rotational spectra of the 1:1 complex showed a planar structure with a bent O−H···N hydrogen bond. The higher symmetry inherent in pyrazine−water generated perturbations in the rotational spectrum which supplied information on the potential energy shape of large-amplitude motions of the water moiety. Available theoretical calculations were not satisfactory both for the conformational minimum and for the shape of the hydrogen bond.[8] For example, in the case of pyrimidine−water the minimum resulted in a nonplanar conformer, in contrast with the experimental evidence.[7]

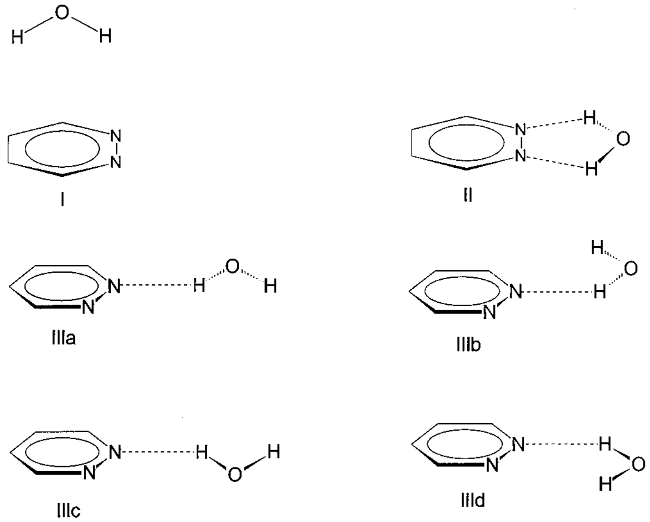

Figure 1. The six plausible conformers for the PRD−water adduct. Species **IIIa** is the observed one.

In the pyridazine ring (PRD) two nitrogen atoms are in adjacent positions. This provides a further possibility for the conformation of its adduct with water, with respect to those of pyrazine−water and pyrimidine−water: water linked with a double hydrogen bond to the two ring nitrogens, forming a five-membered ring. All plausible configurations of the complex are shown in Figure 1. While adducts of PRD with methane and ammonia have been observed in a supersonic molecular jet expansion by two-color time-of-flight mass spectroscopy,[9] this technique did not work for the adduct with water. The weak interactions of PRD with rare gas atoms have been characterized by the rotational spectra of its complex with argon.[8] The centrifugal distortion parameters derived from the rotational spectrum contain information on the dynamics and on the vibrational van der Waals modes which was extracted by using an appropriate model that inverts directly the spectrum to the potential energy parameters.

In this work we report the first experimental observation of the 1:1 complex between pyridazine and water (PRD−W) through the analysis of its rotational spectra in a supersonic expansion. The aim of this study is to establish experimentally the structure of the isolated complex and to arrive at an understanding of the intermolecular interactions governing the

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association process which can be regarded as a prototype for the solvation of heterocyclic aromatic rings containing nitrogen.

Experimental Details

The Stark and pulse modulated free jet absorption millimeter-wave spectrometer used in this study has already been described elsewhere.[11,12] It works in the range 53−78 GHz with the following detection scheme: (a) first phase detection at 33 kHz using a time constant sufficiently low to allow the detection of the effect of pulsing; (b) final phase detection at the pulse frequency and suitable time constant in relation to the frequency scanning speed.

The sample of PRD was purchased from Aldrich and used without further purifications. Since PRD does not have enough vapor pressure at room temperature (bp 208 °C) for our experiments, the sample needed to be heated, as described below.

The conditions were optimized for the 1:1 adduct formation. Argon at a pressure of 0.4 bar was flowed over water at room temperature and then through the furnace containing PRD at 60 °C. The mixture was then expanded to about 5×10^{-3} mbar through a pulsed nozzle (repetition rate 5 Hz) with a diameter of 0.35 mm, reaching an estimated "rotational" temperature of about 10 K. The high speed of the scans (10 GHz/day) and the preserved natural intensity of lines allow rapid acquisition of spectra and simplify their assignment.

Assignment and Characteristics of the Spectra

Three different kinds of H bonds are plausible for PRD−W, as shown in Figure 1. In **I** the π-cloud acts as a proton acceptor, while in **II** (bifurcated H bond) and **III** the nitrogen lone pair(s) do so. Due to the *syn* (*S*) or *anti* (*A*) position of the second ring nitrogen (N_2) with respect to the water oxygen and to the *zusammen* (*Z*) or *entgegen* (*E*) configuration of the hydrogen bond and the nonbonded water hydrogen, four possible planar conformations may be anticipated for form **III** of the complex (**IIIa**, **IIIb**, **IIIc**, and **IIId**; see Figure 1). The first estimate of the rotational constants was obtained by assuming the water molecule to be bound to the nitrogen atom (N_1) of PRD in a way similar to that in pyrazine−water[6] and pyrimidine−water,[7] i.e., form **IIIa** (*AE*, planar) with a bent O−H···N hydrogen bond ($\angle$NHO $\cong$ 152° and $r_{H\cdots N} \cong$ 1.94 Å). The geometries of PRD[13] and water[14] were assumed to remain unaltered in the complex. The spectrum was predicted to be that of a near symmetric prolate rotor with two components of the dipole moment along the *a* and *b* inertial axes. At the rotational temperature achieved with the free jet the strongest transitions were expected to be R-branch μ_b-type, with J ranging from 6 to 15 in our frequency range; they were in fact assigned. Rotational spectra of isotopomers of PRD−water with D_2O and $H_2{}^{18}O$ were then recorded. No hyperfine structure due to the presence of the two ^{14}N nuclear quadrupoles or to large-amplitude water motions was observed.

The absence of any vibrational splitting suggests that the water unit is quite "rigid" in this complex. The measured frequencies of millimeter-wave rotational transitions are reported in Table 1. They have been fitted with Watson's *S*-reduced Hamiltonian[15] in representation I^r. The rotational and centrifugal distortion constants determined for the three isotopomers are listed in Table 2.

TABLE 1: Measured Transition Frequencies (MHz) in the Millimeter-Wave Rotational Spectrum of PRD−Water

$J'(K'_aK'_c)-J''(K''_aK''_c)$	H_2O	D_2O	$H_2{}^{18}O$
6(6)−5(5)[a]	67727.98	67271.33	67635.95
7(5)−6(4)[a]	61083.24	60392.91	60680.91
7(6)−6(5)[a]	70439.33	69830.98	70190.55
8(6)−7(5)[a]	73149.01	72389.29	72744.00
8(7)−8(6)[a]		61316.78	
9(6)−8(5)[a]	75856.29	74945.61	75295.26
9(7)−9(6)[a]	60757.18	61302.29	61768.36
10(4,7)−9(3,6)	59513.79		
10(4,6)−9(3,7)	59932.24		
10(5,6)−9(4,5)	69174.00	68038.90	
10(5,5)−9(4,6)	69188.44	68047.89	
10(6)−9(5)[a]		77499.03	77843.77
10(7)−10(6)[a]		61283.30	61749.45
11(4,8)−10(3,7)	61955.16	60735.89	60946.58
11(4,7)−10(3,8)	62725.14	61282.78	61473.51
11(5,7)−10(4,6)	71844.73	70567.79	70837.45
11(5,6)−10(4,7)	71878.92		70857.81
11(7)−11(66)[a]		61259.13	61725.50
11(8)−11(7)[a]		70722.68	
12(4,9)−11(3,8)	64257.82	62990.69	63205.44
12(4,8)−11(3,9)	65583.93	63936.84	64117.89
12(5,8)−11(4,7)	74491.19	73079.23	
12(5,7)−11(4,8)	74564.00	73125.10	73388.79
12(7)−12(6)[a]	60666.18	61228.51	61695.31
12(8)−12(7)[a]		70700.43	
13(4,10)−12(3,9)	66383.92	65108.84	65331.46
13(4,9)−12(3,10)	68541.94	66658.46	66827.00
13(5,9)−12(4,8)	77101.93	75565.40	75828.61
13(5,8)−12(4,9)	77246.81	75656.50	75915.14
13(7)−13(6)[a]	60618.86	61190.45	61657.75
14(4,11)−13(3,10)	68299.70	67059.21	67293.74
14(4,10)−13(3,11)	71640.89	69477.89	69629.65
14(5,10)−13(4,9)		78015.55	78277.34
14(5,9)−13(4,10)		78186.92	
14(7)−14(6)[a]		61143.57	61611.61
15(4,12)−14(3,11)	69982.25		
15(4,11)−14(3,12)	74931.77	72431.99	
15(7)−15(6)[a]	60490.66		

[a] Doubly overlapped transitions due to the near prolate degeneracy of the involved levels: only K_a is given.

TABLE 2: Rotational and Centrifugal Distortion Constants ("*S*" Reduction and I^r Representation) and Inertial Defects of PRD−Water

	normal	D_2O	$H_2{}^{18}O$
A/MHz	6033.91(2)[a]	5999.346(9)	6032.72(2)
B	1505.74(1)	1414.53(1)	1411.17(1)
C	1205.02(2)	1145.03(1)	1143.60(1)
D_J/kHz	0.52(2)	0.46(2)	0.50(2)
D_{JK}	17.30(4)	15.33(4)	15.90(4)
D_K	−16.3(4)	−13.3(2)	−13.9(3)
d_1	−0.16(2)	−0.14(3)	−0.20(3)
d_2	−0.08(1)	−0.05(1)	−0.051(8)
N[b]	29	33	26
σ (MHz)	0.07	0.07	0.05
Δ_{cc} (u Å^2)	0.01	−0.14	0.02

[a] Errors in parentheses are expressed in units of the last digit. [b] Number of transitions in the fit.

The Geometry of PRD−Water

The small values of the ground-state inertia defect $\Delta_i = 0.01$, −0.14, and 0.02 u Å^2 for the normal, D_2O, and $H_2{}^{18}O$ species, respectively, suggest planar or near-planar geometry of the complex. The overall planarity is in accord also with the observation of μ_b, but no μ_c-type transitions. Forms **I** and **II** of Figure 1 are ruled out because the first is not planar, and the second one would have only μ_a-type transitions. The changes in (B + C) in going from the normal to the D_2O species allow the *AZ* and *SZ* conformers (**IIIb** and **IIId** of Figure 1) to be ruled out. It is more difficult, just on the basis of the available rotational constants, to discriminate between the *AE* and *SE* (**IIIa** and **IIIc** of Figure 1) species. Nevertheless, the ab initio

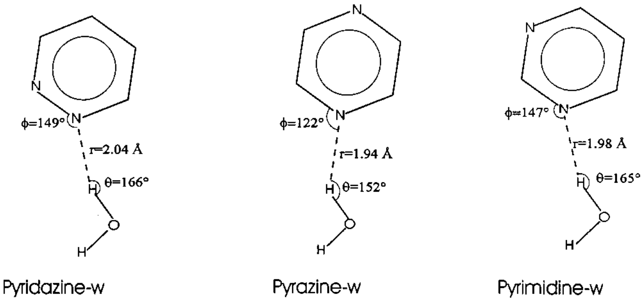

Figure 2. Comparison among the H bond geometries for the observed, planar, conformers (*AE*) of the complexes of diazines with water.

TABLE 3: r_0 H Bond Parameters (H′ Participates in the Hydrogen Bond) Obtained Fixing the Geometries of Water and PRD to the Values of the Isolated Molecules[a]

(1) r_0 Hydrogen Bond Parameters (Å and deg, See Figure 1)[b]

$r_{N-O} = 2.966(3)$[c] $\angle NNO = 153.8(3)$ $\angle NOH' = 10(2)$ Rd = 4.08

(2) r_s Coordinates of the O Atom (Å)

|*a*|		|*b*|		|*c*|	
exptl	calc[e]	exptl	calc[e]	exptl	calc[e]
3.385(1)	3.399	0.12(3)	0.09	0.06(6)	0.0

(3) Rotation Constants

	normal		D_2O		^{18}O	
(MHz)	exptl	calc[e]	exptl	calc[e]	exptl	calc[e]
A	6033.9	6033.8	5999.3	6000.0	6032.7	6032.7
B	1505.7	1506.5	1414.5	1414.5	1411.2	1411.1
C	1205.0	1205.5	1145.0	1144.7	1143.6	1143.6

[a] The experimental substitution coordinates of the O atom and rotational constants are compared to the values calculated with this refined geometry. [b] The alternative set, shown in Figure 2, is $r_{N-H} = 2.04$, $\angle NNH' = 149.2(3)°$, and $\angle NH'O = 165.5°$. [c] Errors (in parentheses) are expressed in units of the last digit. [d] Distance between the centers of mass of the monomers. [e] Calculated with the r_0 structure (see top of the table and text).

calculations[8] and the favorable dipole−dipole interaction energy (the dipole moments of the two subunits tend to be antiparallel) of the *AE* (**IIIa**) form strongly indicate this one to be the most favorite one, similarly to the case of pyrimidine−water.[7]

The r_0 structures of the H bond parameters, obtained fitting the O−N distance and the NNH′ and NOH′ angles of Figure 2(H′ participates in the H bond) while keeping the geometries of the two subunits fixed, are reported in Table 3, together with the experimental and calculated values of the rotational constants. The same comparison is also reported for the r_s, coordinates of the oxygen atom, obtained by applying Kraitchmann's equations.[16] They confirm the conformational interpretation given above but cannot rule out conformation **IIIc**, for which a similar agreement can be obtained.

The main H bond structural parameters of the complexes of the three diazines with water are shown in Figure 2. In the cases of PRD−W and pyrimidine−water the $N_2N_1 \cdots H$ and $C_2N_1 \cdots H$ angles are much larger than 120°, to reach a nearly antiparallel orientation of the dipole moments of the two moieties.

Internal Motions

The three translational and the three rotational degrees of freedom of the isolated water molecule are replaced by six low-energy vibrational modes upon formation of the complex. One of these motions is the stretching motion between the two constituent molecules, while the remaining modes can be classified as two intermolecular bends and three internal rotations or torsions of the water moiety.

The intermolecular stretch is sufficiently well isolated from the other low-frequency motions so that meaningful hydrogen bond stretching constants are obtained by approximating the complex to a diatomic. Enhanced formulas of this type have been developed by Millen for linear and symmetric top complexes[17] and by Read et al.[18] for asymmetric top complexes in which the stretching coordinate is near-parallel to the inertial *a*-axis. This condition is satisfied for PRD-W, so that the equation

$$k_s = 16\pi^4(\mu_D R_{CM})^2[4B_D{}^4 + 4C_D{}^4 - (B_D - C_D)^2(B_D + C_D)^2]/(hD_J) \quad (1)$$

can be used to derive the hydrogen bond stretching force constant k_s. The subscript D denotes a dimer quantity, μ_D is the pseudodiatomic reduced mass, R_{CM} is the distance between the centers of mass of the monomers (4.13 Å for PRD−W), and D_J is the centrifugal distortion constant. For PRD−W $k_s = 13.1$ N m^{-1} and corresponds to a stretching frequency of 123 cm^{-1}. This is comparable to $k_s = 13.8$ N m^{-1} for pyrimidine−water,[7] so that the dimerization energy should be close to the value of $\Delta E = 21.4$ kJ/mol for that complex. The k_s comparison with pyrazine−H_2O cannot be made reliably since its value of D_J is perturbed by large-amplitude motions.

Comparison among the Diazine−Water Complexes and Conclusions

The present work concludes the investigations of the rotational spectra of the 1:1 complexes of diazines with water. In contrast to the benzene−water complex, where water lies above the ring plane with a $\pi \cdots H-O$ H bond,[4,5] all three diazines form planar complexes characterized by an $N \cdots H-O$ H bond. Nevertheless, the three rotational spectra show important differences: for example, the symmetry properties of pyrazine are somehow preserved in pyrazine−water[6] and produce a systematic doubling of lines which supplies information for the determination of the barrier to internal rotation of the water subunit. PRD−W and pyrimidine−water[7] are rather similar to each other: in both cases the dipole moments of the water and of the diazine part tend to adopt an antiparallel orientation in order to have a favorable dipole−dipole interaction energy. As a result, a strong distortion of the $X_2N_1 \cdots H$ (X = C or N) angle is observed (see Figure 2 and Table 3). Since this antiparallelism is more difficult to be achieved in the case of PRD−W, a higher distortion, and then a lower dissociation energy, is required in this case.

The experimental moments of inertia of the three isotopomers of PRD−water indicate that the ground state is located either in the single global minimum with *AE* configuration or well above a small barrier between two possible nearby nonplanar minima. The remaining *AZ*, *SE*, and *SZ* configurations could correspond to local minima; in this case they would easily relax to the *AE* global minimum during the supersonic expansion, as shown by Godfrey et al. for small interconversion barriers.[19]

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